REMARKS

Claims 236-342 were pending as of the mailing of the Office Action on December 8, 2003. The Office Action required election of any of the following sets of claims: (Group I) claims 236-248 and 316-342, directed to a method for increasing Nitric Oxide production in a subject by administering an HMG-CoA reductase inhibitor; (Group II) claims 249-261, directed to a method for attenuating the downregulation of Nitric Oxide production by administering an HMG-CoA reductase inhibitor; (Group III) claims 262-275, directed to a method for treating a nonhypercholesterolemic or nonhyperlipidemic subject with a cardiovascular disease or disorder by administering an HMG-CoA reductase inhibitor; (Group IV) claims 276-290, directed to a method for treating a cerebrovascular disease or disorder by administering an HMG-CoA reductase inhibitor; (Group V) claims 291-304, directed to a method for increasing cerebral blood flow in a cerebral tissue by administering an HMG-CoA reductase inhibitor; (Group VI) claims 305-315, directed to a method for increasing Nitric Oxide Synthase activity in a subject by administering an HMG-CoA reductase inhibitor and a Nitric Oxide Synthase substrate; and (Group VII) claims 328-342, directed to a method for treating an inflammatory disease or disorder by administering an HMG-CoA reductase inhibitor. The Office Action further required election of a single disclosed species of HMG-CoA reductase inhibitor for examination.

As indicated in the Office Action, during a telephone conversation with Ms. Danielle Herritt on November 12, 2003, Applicants made a provisional election to prosecute Group III (claims 262-275) with simvastatin as a species election. Applicants confirm that they elect to prosecute Group III (claims 262-275) with simvastatin as a species election. Accordingly, claims 236-261 and 276-342 are withdrawn from consideration, without prejudice to their entry and prosecution in subsequently filed continuation or divisional applications.

Claims 262-275 have been rejected. Claim 268 has been canceled without prejudice. Claim 262 is amended to incorporate the limitation of claim 268. Support for this amendment can be found throughout the specification, for example, on page 22, lines 3-4, and in the originally filed claims. Claim 265 is amended to correct a spelling error.

Support for this amendment can be found on page 24, line 22 of the originally filed application.

The foregoing amendments and cancellation should in no way be construed as an acquiescence to any of the Examiner's rejections and have been made solely to expedite examination of the present application. No new matter has been added. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s). After entry of these amendments, claims 262-267 and 269-275 are pending in this application.

Rejection Under 35 U.S.C. § 102(e)

In the Office Action dated December 8, 2003, claims 262-267, 269-271 and 273 were rejected under 35 U.S.C. § 102(e) as being anticipated by US Patent No. 6,465,516 B1 to Kaesemeyer (Kaesemeyer).

In order to expedite examination, claim 262 has been amended to incorporate dependent claim 268, directed to the administration of HMG-CoA reductase inhibitors in a sustained release delivery system, a delayed release delivery system or a time release delivery system. The limitation of claim 268 is not taught or suggested by Kaesemeyer. Accordingly, reconsideration and withdrawal of the rejection of claim 262 and its respective dependent claims, are respectfully requested.

Rejection Under 35 U.S.C. § 103 (Kaesemeyer in view of Dansereau et al.)

The Examiner rejects claims 268, 269, 272 and 273 under 35 U.S.C. § 103(a) as being unpatentable over Kaesemeyer in view of US Patent No. 5,622,721 to Dansereau *et al.* (Dansereau). Applicants respectfully traverse.

The outstanding rejection appears to be based on the premise that Kaesemeyer teaches the treatment of nonhypercholesterolemic or nonhyperlipidemic subjects with a cardiovascular disease or disorder by administering an HMG-CoA reductase inhibitor and Dansereau teaches sustained release and delayed release formulations. As such, according to the Examiner, the combination of the references renders the claimed invention obvious.

Applicants respectfully disagree. As the Examiner is well aware, in order to combine prior art references to render a claim obvious, there must be a suggestion or

motivation to combine the references, *i.e.*, the references must suggest the desirability of the combination. Kaesemeyer does not suggest or provide motivation for use of any sort of sustained release, time release or delayed release formulation of HMG-CoA reductase inhibitor. Similarly, Dansereau does not suggest or provide motivation for use of its sustained and delayed release formulations with HMG-CoA reductase inhibitors. Indeed, the formulations of Dansereau are specific to risedronate. Moreover, the formulations of Dansereau are motivated by a desire to target a particular problem, namely the tendency of risedronate to irritate the upper gastrointestinal tract. Dansereau therefore provides a sustained release or delayed release formulation that allows for release of risedronate in the lower gastrointestinal tract, for example, through the use of enteric coatings, in order to avoid irritation in the upper gastrointestinal tract. By comparison, HMG-CoA reductase inhibitors are not known to cause irritation in the upper gastrointestinal tract. Accordingly, there is no suggestion or motivation to use the sustained or delayed release formulations of Dansereau with HMG-CoA reductase inhibitors. In fact, Dansereau teaches away from such a combination, by teaching that the formulations target a particular problem that HMG-CoA reductase inhibitors do not involve.

As such, there is no motivation or suggestion to combine Kaesemeyer and Dansereau. In turn, the claims, as now amended, are not rendered obvious by the prior art references. Accordingly, Applicants respectfully request withdrawal of the rejection of the pending claims under 35 U.S.C. § 103.

Rejection Under 35 U.S.C. § 103 (Kaesemeyer in view of Birkmayer et al.)

The Examiner rejects claims 274 and 275 under 35 U.S.C. § 103(a) as being unpatentable over Kaesemeyer in view of US Patent No. 5,668,114 to Birkmayer *et al.* (Birkmayer). In light of the amendment to claim 262 presented herein, this § 103(a) rejection is rendered moot. Neither Kaesemeyer nor Birkmayer disclose the use of a sustained, delayed or time release delivery system for administration of HMG-CoA reductase inhibitors. In turn, the claims, as amended, are not rendered obvious by the prior art references. Accordingly, Applicants respectfully request withdrawal of the rejection of the pending claims under 35 U.S.C. § 103.

CONCLUSION

In view of the foregoing remarks, reconsideration of the rejections and allowance of all pending claims is respectfully requested. If there are any remaining issues or if the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Dated: June 8, 2004

Respectfully submitted,

By _____

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